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Gender, Alcohol Consumption, and Renal Cell Carcinoma

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The nature of the association between alcohol consumption and renal cell carcinoma (RCC) is not well understood, but there are indications of effect modification by gender. The authors report data from a population-based case-control study conducted in Iowa from 1986 to 1989. RCC cases (261 men and 145 women) were identified through the Iowa Cancer Registry, while controls (1,598 men and 831 women) were randomly selected from the general population, frequency matched on age and gender. Subjects provided detailed information on a mailed questionnaire regarding demographic, anthropometric, lifestyle, dietary, and medical history risk factors. In age-adjusted analysis, there was a decrease in risk for women who reported consuming more than three servings (median among drinkers) of alcohol per week (odds ratio = 0.5, 95% confidence interval: 0.2, 0.9) compared with never drinkers. No evidence of an association among men was noted (odds ratio = 1.1, 95% confidence interval: 0.8, 1.5). Multivariate adjustment for anthropometric, lifestyle, smoking, and dietary factors did not alter the findings. Analysis by type of alcohol suggested that the inverse association was strongest for beer consumption, but estimates were imprecise. These findings suggest an inverse association of alcohol consumption and RCC development among women but not among men. *Am J Epidemiol* 2002;155:455–62.

alcohol drinking; carcinoma, renal cell; case-control studies

Whether alcohol consumption plays a role in the development of renal cell carcinoma (RCC) remains unclear. Several ecologic studies (1–3) have suggested a positive association between intake of alcohol and development of RCC, but only one case-control study has reported a positive association (4). Indeed, most case-control (5–10) and cohort (11–15) studies show no association of RCC with alcohol consumption.

While the majority of studies suggest no overall association, there is some evidence of an inverse association between alcohol consumption and RCC development in women specifically. Investigators from a large, international, multicenter case-control study of RCC (16) reported that drinking alcohol at least once a week was not associated with RCC in men (odds ratio (OR) = 1.0, 95 percent confidence interval (CI): 0.8, 1.3) but was linked to significantly decreased RCC risk in women (OR = 0.6, 95 percent CI: 0.5, 0.8). In addition, the authors noted a dose-response trend with number of total drinks per week among women. Data from prospective studies supporting an inverse association of alcohol and RCC among women are limited but do exist (17). Given that there are recognized gender-related differences in the metabolism of alcohol (18), further study is warranted.

The intent of this investigation is to address the potential for a gender-specific association of alcohol consumption and RCC development after adjustment for accepted and newly identified confounding factors. To do this, we used data from a population-based case-control investigation conducted in Iowa from 1986 to 1989. We also report the individual associations for specific types of alcohol (beer, wine, and liquor).

MATERIALS AND METHODS

Study population

Full details of this study are reported elsewhere (19). Briefly, we conducted a population-based case-control investigation of cancer occurrence at six anatomic sites (pancreas, bladder, kidney, brain, colon, and rectum). The state of Iowa was chosen as the site for this study in part because of the availability of cancer incidence data from the Iowa Cancer Registry (ICR), a participant in the National Cancer Institute's Surveillance, Epidemiology, and End Results Program (20). Eligible cases were residents of Iowa who were aged 40–85 years and newly diagnosed with histologically confirmed RCC. Those with a previous diagnosis of a malignant neoplasm, except basal and squamous cell

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Abbreviations: BMI, body mass index; CI, confidence interval; ICR, Iowa Cancer Registry; OR, odds ratio; RCC, renal cell carcinoma.

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carcinomas of the skin, were excluded. Cases were identified from 1985 to 1987 by the ICR, with supplementation by a rapid reporting system in 1987. Of the 463 RCCs identified by the ICR for the study, 406 (88 percent) responded, with 93 (23 percent) requiring proxy respondents to provide information.

Controls under age 65 years were randomly selected from computerized state driver's license records. Controls aged 65 or older were selected randomly from listings provided by the US Health Care Financing Administration. Both of these selection rosters have been shown to achieve greater than 95 percent coverage of the intended population (21, 22). As with cases, controls with a history of cancer, other than nonmelanoma skin cancer, were excluded. Controls were frequency matched to cases by gender and 5-year age group. Of the 999 controls under age 65 years identified, 817 (82 percent) participated, while 1,617 of 2,036 (79 percent) of the identified controls aged 65 years or over participated. All but two controls were direct respondents rather than proxies.

Data collection

Data were collected with a mailed questionnaire supplemented by a telephone interview. The questionnaire assessed major and proposed RCC risk factors, including demographics, anthropometric measures at various times in life, smoking history and status, medical history (including self-report of a physician-diagnosed history of hypertension), reproductive factors, occupational history, usual physical activity (nonoccupational), and family history of cancer. Also included in the questionnaire was a 55-item food frequency section.

Information regarding the consumption of alcohol was ascertained in a portion of the food frequency questionnaire in which participants were asked to report their usual consumption over all adult years of the following: beer (12-ounce (591.4-ml) can), wine (4-ounce (118.3-ml) glass), and liquor (one shot). Participants were specifically instructed to ignore recent changes in alcohol consumption.

Statistical analysis

Usual adult consumption of alcohol was first dichotomized as never and ever drinkers. In addition, we summarized alcohol consumption by total servings of alcohol consumed per week. This variable was then categorized a priori based on the median split among drinkers into three levels: nondrinkers, less than three servings per week, and three or more servings per week. Individual types of alcohol (beer, wine, and liquor) were stratified in the same manner as servings per week, with nondrinkers of the particular type of alcohol as the reference group. We also analyzed the types of alcohol by utilizing nondrinkers of any alcohol as the referent group; results were similar. Finally, since the actual amount of alcohol (in grams) differs across the three alcohol beverage types, we also summarized alcohol consumption in grams per week by using the following standard values for our calculations: one 12-ounce beer = 12 g; one shot of liquor = 14 g; one 4-ounce glass of wine = 9.6 g. This variable (g/week) was then also categorized a priori based on the median split among drinkers.

Odds ratios and 95 percent confidence intervals were used to estimate the association of alcohol consumption and RCC. We used unconditional logistic regression to estimate both age- and multivariate-adjusted odds ratios. Tests for trend across levels of alcohol consumption were conducted by treating each ordinal score variable (0, 1, 2) as a continuous variable in the logistic regression model. We also tested for trends by modeling alcohol consumption as a continuous variable. No differences were noted between the two methods; therefore, we report results based on the tests involving the ordinal score variable. Analyses were first performed on the entire dataset and then repeated, stratifying by gender. Decisions regarding confounding factors in multivariate analysis were based on 1) whether or not the covariate was associated with both alcohol consumption and RCC development, and 2) what effect inclusion of the particular covariate had on the risk estimate for alcohol consumption. Multivariate model building was performed separately for men and women to allow for sex-specific confounding factors (i.e., body mass index (BMI) is a stronger risk factor for RCC among women than among men). We also conducted a separate analysis in which we removed any next-of-kin respondents (women, $n = 23$; men, $n = 72$). The results did not differ between the two methods; therefore, we report findings including all respondents. Of note, tests for interaction with other known risk factors for RCC (BMI, hypertension, and smoking) did not suggest that any of these factors altered the effect of alcohol on RCC risk. Statistical analyses were performed using the PROC LOGISTIC procedure in SAS version 8.0 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

After exclusion of subjects who lacked information on alcohol consumption, there were 406 cases of RCC (261 men (64 percent) and 145 women (36 percent)) and 2,429 controls (1,598 men (66 percent) and 831 women (34 percent)) available for this analysis. Table 1 summarizes the differences between cases and controls with regard to potential confounding factors. Cases were younger, more likely to be heavy smokers (greater than 40 pack-years), and more likely to have a BMI of greater than 29 kg/m^2. A history of hypertension was more likely to be reported among cases, as was a positive family history (RCC in a first-degree relative) and a history of bladder infections. Cases were slightly less likely to report exercising once a day. Consumption of fruits and vegetables was higher among controls, although cases consumed more servings of red meat per week. Two deviations from the overall results in table 1 were noted when gender-specific associations were considered (data not shown): 1) There was no difference between male cases and controls with regard to BMI level ($p = 0.4$), and 2) pack-years of smoking was not associated with case-control status among women ($p = 0.5$).

TABLE 1. Relation of potential confounding factors to case-control status, Iowa, 1986–1989

Factor	Controls (n = 2,429)		RCC† cases (n = 406)		p value*
	Mean (SD†)	%	Mean (SD)	%	
Age (years)	68 (9.9)		64 (9.6)		0.001
Red meat (servings/week)‡	9.8 (7.3)		10.6 (6.5)		0.05
Fruit (servings/week)‡	17.2 (12.8)		14.8 (10.6)		0.0002
Vegetables (servings/week)‡	27.0 (15.3)		24.0 (12.1)		0.0001
BMI† (kg/m^2)					
<24		37.5		32.1	
24–29		30.4		28.6	
>29		32.1		39.3	0.02
Pack-years of smoking					
None		43.3		34.7	
1–20		15.1		13.4	
21–39		15.2		16.8	
≥40		26.4		35.1	0.001
History of hypertension					
No		63.7		52.0	
Yes		36.3		48.0	0.0001
Family history of kidney cancer					
No		99.0		97.0	
Yes		1.0		3.0	0.002
Nonoccupational physical activity					
Never		33.7		39.1	
1–4/month		16.0		18.8	
2–6/week		30.0		28.0	
1/day		20.3		14.1	0.01
History of bladder/kidney infection					
No		78.1		66.1	
Yes		21.9		33.9	0.001

* p value is either for global test for differences among means or chi-square test for differences in proportions, as appropriate.
† RCC, renal cell carcinoma; SD, standard deviation; BMI, body mass index.
‡ Adjusted for total energy intake.

Table 2 presents mean values and percentages of potential confounding factors across levels of alcohol consumption (servings per week) among the controls. Those who consumed three or more servings of alcohol per week were younger and more likely to be heavy smokers (>40 pack-years). Only slight differences were noted across levels of alcohol consumption for a history of hypertension; exercise; history of bladder or kidney infection; and dietary intake of red meat, fruit, and vegetables. No differences were noted across levels of alcohol consumption for BMI level or family history of kidney cancer. No deviations from the overall results in table 2 were noted when gender-specific associations were considered (data not shown), with the exception that alcohol consumption was associated with a lower BMI among women ($p = 0.004$) but not among men ($p = 0.5$). Specifically, 35 percent of female never drinkers were classified as obese (BMI > 29 kg/m^2) compared with 29 percent of those who consumed three or fewer servings of alcohol per week and only 16 percent of those who consumed more than three alcohol servings per week.

The formal test for an interaction between gender and alcohol consumption (servings per week) suggested that the association between alcohol and RCC was not the same for men and women in our study ($p = 0.03$). Therefore, age- and multivariate-adjusted odds ratios for various measures of alcohol consumption stratified by gender are presented in table 3. Among men, we found a slight age-adjusted increase in risk of RCC for ever drinkers (OR = 1.2, 95 percent CI: 0.9, 1.6), but there was no evidence of a trend in risk with increasing servings per week or grams per week of alcohol consumption ($p = 0.6$). In addition, no particular type of alcohol was associated with development of RCC. Multivariate adjustment for pack-years of smoking, exercise, history of hypertension, history of bladder infection, family history of kidney cancer, and dietary consumption of red meat and fruit had minimal influence on the results.

TABLE 2. Distribution of potential confounding factors among controls by level of usual adult alcohol consumption, Iowa, 1986–1989

Factor	Alcohol consumption (servings/week)						
	Never drinker	%	≤ 3	%	>3	%	*p* value*
Age (years)	69.8		66.0		65.1		0.0001
Red meat (servings/week)†	9.7		9.8		10.5		0.09
Fruit (servings/week)†	17.4		17.3		15.1		0.0008
Vegetables (servings/week)†	27.3		26.2		25.6		0.08
BMI‡ (kg/m^2)							
<24		37		34		39	
24–29		29		32		31	
>29		34		34		31	0.3
Pack-years of smoking							
None		54		38		19	
1–20		12		18		17	
21–39		12		17		20	
≥40		21		27		43	0.001
History of hypertension							
No		60		63		65	
Yes		40		37		35	0.09
Family history of kidney cancer							
No		98		99		98	
Yes		2		1		2	0.4
Nonoccupational physical activity							
Never		37		31		33	
1–4/month		13		20		19	
2–6/week		27		33		31	
1/day		22		17		17	0.001
History of bladder/kidney infection							
No		75		76		80	
Yes		25		24		20	0.03

* *p* value is either for global test for differences among means or chi-square test for differences in proportions, as appropriate.
† Adjusted for total energy intake.
‡ BMI, body mass index.

We found a small, age-adjusted decrease in RCC risk among women who reported ever drinking alcohol (OR = 0.8, 95 percent CI: 0.5, 1.1). Upon further analysis, there was evidence of a decreasing trend in risk with increasing servings of alcohol per week (p for trend = 0.05) and increasing grams of alcohol per week (p for trend = 0.06). Women who consumed more than three alcohol servings per week showed a significant reduction in RCC risk compared with never drinkers (OR = 0.5, 95 percent CI: 0.2, 0.9). A similar result was noted for women categorized in the highest level of grams of alcohol per week (OR = 0.5, 95 percent CI: 0.2, 1.0). Analysis by type of alcohol suggested a possible specific association with beer consumption; however, estimates were based on a small number of cases (n = 5 in the highest category of beer consumption). Multivariate adjustment for remaining type of alcohol; BMI; pack-years of smoking; family history of kidney cancer; and dietary consumption of red meat, fruit, and vegetables did not modify the result.

DISCUSSION

Evidence from this population-based case-control investigation supports an inverse association of alcohol consumption and RCC development among women but not among men. After multivariate adjustment, there was no evidence of a trend with intensity of alcohol consumption among men, either overall or by specific type. In contrast, after multivariate adjustment for known confounders, there was a suggestion of an inverse association with ever drinking alcohol among women. Further, when measures of intensity of alcohol consumption were considered, risk of RCC decreased as alcohol consumption increased. Women categorized in the highest levels of alcohol consumption (either servings/week or g/week) had substantial reductions in RCC risk compared with never drinkers. Among types of alcohol, beer intake appeared to be more important than other forms of alcohol, but numbers were small and confidence intervals were wide.

TABLE 3. Age-adjusted and multivariate risks of RCC* according to usual adult consumption of alcoholic beverages, Iowa, 1986–1989

	Men						Women					
	No. of cases	No. of controls	OR*,†	95% CI*	OR‡	95% CI	No. of cases	No. of controls	OR*	95% CI	OR§	95% CI
Any alcohol												
Never	98	736	1.0		1.0		93	513	1.0		1.0	
Ever	163	862	1.2	0.9, 1.6	1.0	0.7, 1.5	52	318	0.8	0.5, 1.1	0.8	0.5, 1.2
Servings/week												
None	98	736	1.0		1.0		93	513	1.0		1.0	
≤3	80	405	1.3	0.9, 1.8	1.2	0.8, 1.8	43	229	0.9	0.6, 1.3	1.0	0.6, 1.5
>3	83	457	1.1	0.8, 1.5	0.9	0.6, 1.3	9	89	0.5	0.2, 0.9	0.4	0.2, 1.0
p for trend				0.6		0.5				0.05		0.04
g/week												
None	98	736	1.0		1.0		93	513	1.0		1.0	
≤35	77	362	1.4	1.0, 1.9	1.3	0.9, 1.9	41	217	0.9	0.6, 1.3	1.0	0.6, 1.5
>35	86	500	1.2	0.8, 1.5	0.9	0.6, 1.3	11	101	0.5	0.3, 1.0	0.4	0.2, 0.9
p for trend				0.6		0.5				0.06		0.04
Wine (8-ounce¶ glass/week)												
Nondrinker of wine	197	1,223	1.0		1.0		110	625	1.0		1.0	
≤0.5	32	223	0.8	0.5, 1.2	0.8	0.5, 1.3	24	137	0.9	0.5, 1.4	1.0	0.6, 1.7
>0.5	32	152	1.1	0.7, 1.7	1.2	0.7, 2.0	11	69	0.8	0.4, 1.5	0.9	0.5, 1.9
Beer (12-ounce¶ can/week)												
Nondrinker of beer	127	924	1.0		1.0		122	702	1.0		1.0	
≤1	56	261	1.3	0.9, 1.9	1.4	0.9, 2.0	18	73	1.2	0.7, 2.1	1.3	0.7, 2.3
>1	78	413	1.1	0.8, 1.6	1.0	0.7, 1.4	5	56	0.5	0.2, 1.1	0.3	0.2, 1.0
Liquor (1-ounce¶ shot/week)												
Nondrinker of liquor	153	1,051	1.0		1.0		118	673	1.0		1.0	
≤1	57	267	1.3	0.9, 1.8	1.4	1.0, 2.1	17	103	0.8	0.5, 1.4	0.9	0.5, 1.6
>1	51	280	1.1	0.8, 1.6	1.1	0.7, 1.6	10	55	1.0	0.5, 2.0	1.1	0.5, 2.2

* RCC, renal cell carcinoma; OR, odds ratio; CI, confidence interval.
† Adjusted for age.
‡ Adjusted for age, pack-years of smoking, history of hypertension, history of bladder infection, family history of kidney cancer, exercise, consumption of red meat, and consumption of fruit.
§ Adjusted for age; pack-years of smoking; history of hypertension; body mass index (kg/m^2); family history of kidney cancer; and consumption of red meat, fruit, and vegetables.
¶ 1 ounce =29.57 ml.

To date, seven population-based case-control studies have evaluated the association of alcohol and RCC (table 4). Of these, only five had detailed enough exposure data from which to draw meaningful conclusions. Three of these five studies (7, 10, 23) reported no significant association between alcohol consumption and RCC development, while the two remaining studies (16, 24) showed an inverse association with alcohol consumption. In a study involving 315 cases and 336 population controls, Asal et al. (24) reported a consistent inverse association of alcohol consumption and RCC regardless of gender. The authors also reported an inverse association with wine in both genders ($OR_{ever\ drinkers/men} = 0.5$, 95 percent CI: 0.3, 0.8; $OR_{ever\ drinkers/women} = 0.5$, 95 percent CI: 0.4, 0.9) and hard liquor in men only ($OR_{ever\ drinkers} = 0.6$, 95 percent CI: 0.3, 0.9). In each instance (overall and by alcohol subtypes), the inverse association was not seen among the heaviest drinkers. Data from the largest population-based case-control study on RCC (16) conflict slightly with the findings of Asal et al., in that the inverse association was limited to women and remained at high levels of consumption. Drinking any alcohol at least once per week was not associated with RCC among men (OR = 1.0, 95 percent CI: 0.8, 1.3) but was associated with a decreased risk among women (OR = 0.6, 95 percent CI: 0.5, 0.8). Additionally, among women only, there was a significant decreasing trend in risk of RCC with increasing levels of both total alcohol servings per week (p for trend = 0.0003) and wine servings per week (p for trend = 0.0001).

Data on an alcohol-RCC association from cohort studies are limited. Investigators from studies conducted in the 1970s reported no association between alcohol consumption and RCC mortality (11–14). These studies involved mostly male participants who consumed very large amounts of alcohol (i.e., alcoholics), and their findings were based on low numbers of observed events. More recently, there was no evidence of an association between alcohol consumption and RCC development in a Swedish cohort of 8,340 men and 1,013 women discharged with a diagnosis of alcoholism who were followed up for an average of 8 years (15). Risk estimates were based on 20 observed RCC cases in men and only two in women. Of interest, authors of a large population-based cohort investigation of postmenopausal women in Iowa followed for 6 years found an age-adjusted inverse association between alcohol consumption and RCC incidence (17). Compared with never drinkers, women who reported consuming more than 3.4 g of alcohol per week

TABLE 4. Published population-based case-control studies reporting data regarding alcohol consumption and RCC*

Author (reference) and year	Location	Case:control	Results	Comments
McLaughlin et al. (23), 1984	Minneapolis, MN	495:697	Ever beer: $OR^*_{men} = 1.2$ (95% CI*: 0.8, 1.6), $OR_{women} = 1.6$ (95% CI: 0.8, 3.0); no trend with increasing intensity in either sex	Adjusted for age and smoking (and BMI* in women); no association with wine, liquor, or all alcohol
Yu et al. (5), 1986	Los Angeles, CA	160:160	Data not shown	Cases and controls did not differ significantly for consumption of alcohol
Asal et al. (24), 1988	Oklahoma	315:336	Significant inverse association of ever use of wine (OR ~ 0.5) in both sexes; J-shaped trend in risk with increasing intensity; similar results for all alcohol and liquor	Adjusted for age, smoking, and BMI; when compared with hospital controls, association no longer apparent
MacClure and Willett (7), 1990	Boston, MA	410:605	Moderate vs. low wine consumption: OR = 0.7 (95% CI: 0.4, 1.2); high vs. low wine consumption: OR = 1.0 (95% CI: 0.3, 3.0)	Adjusted for age, sex, and smoking. Moderate = 2–7 glasses/week; high ≥2 glasses/day
McLaughlin et al. (8), 1992	Shanghai, China	154:157	Data not shown	No significant differences seen for consumption of alcohol
Kreiger et al. (10), 1993	Ontario	518:1,381	High vs. low alcohol consumption: $OR_{men} = 1.3$ (95% CI: 0.7, 2.4); $OR_{women} = 0.7$ (95% CI: 0.4, 1.4)	Adjusted for age, smoking, and BMI. No association with type of alcohol
Wolk et al. (16), 1996	Five countries	1,185:1,527	Women drinking >10 alcohol drinks/week: OR = 0.5 (95% CI: 0.3, 0.8); women drinking >3 glasses wine/week: OR = 0.3 (95% CI: 0.1, 0.4)	Adjusted for age, sex, BMI, smoking, and total calories. No association in men. Significant trend in risk among women for both all alcohol and wine

* RCC, renal cell carcinoma; OR, odds ratio; CI, confidence interval; BMI, body mass index.

(median split among drinkers) experienced a significant reduction in RCC risk (age-adjusted relative risk = 0.6, 95 percent CI: 0.2, 0.7).

While our current findings may be due to chance, the growing number of studies reporting an inverse association between alcohol and RCC in women lessens this possibility. In addition, there are examples of factors that impart gender-specific cancer risk (25–27). With regard to RCC, there is evidence that risk factors such as obesity (28, 29), certain occupational exposures (27), and smoking (30) may influence RCC risk differently among men and women. Further, it should be noted that there are documented differences between men and women in the metabolism of alcohol (18). After consuming comparable amounts of ethanol, women have higher blood ethanol concentrations than do men, even after allowing for differences in body size. Finally, when we split the highest grams per week category by the median use in that group (98 g/week), the risk estimates for RCC continued to decrease with increasing alcohol consumption ($OR_{35–98\ g/week} = 0.6$, 95 percent CI: 0.3, 1.4 and $OR_{>98\ g/week} = 0.4$, 95 percent CI: 0.1, 1.2). Despite the lack of precision, our ability to show that risk of RCC continues to decrease when we focus our attention on the heavy drinkers in this population lessens the likelihood that our findings are due to chance.

Gender-specific associations may suggest an underlying hormonal mechanism. However, limited data indicate that estrogens increase, rather than decrease, risk of RCC (28, 31, 32), and the data regarding effects of alcohol on circulating levels of estrogen are inconsistent (33, 34). Of note, there is some evidence that alcohol consumption decreases estrogen metabolism in women (35). If this decrease in metabolism resulted in an overall reduction in the formation of reactive quinones, this could translate into lower risk of RCC for women who consume alcohol compared with those who abstain. Nevertheless, due to conflicting data on the effect of alcohol on the estrogen-catecholestrogen-quinone metabolic pathway, this theory is merely speculative.

We must also seek other explanations for our findings. Nondifferential misclassification of alcohol consumption among men could have masked a true inverse association in men. Similarly, if either female cases or controls incorrectly reported their alcohol consumption in a systematic manner, a false association could have been generated. However, the likelihood that such errors in reporting were responsible for our findings, as well as those of other studies, is suspect. Further, as noted, evidence of an inverse alcohol-RCC association in women has been reported in a large prospective investigation in which recall bias is not a problem.

There are limitations to our study. All exposures were self-reported, and for all dietary factors, including alcohol consumption, respondents were asked to report on usual adult levels of consumption. This prohibits assessment of variation in alcohol consumption over the lifetime of the subjects. In addition, because of a lack of persons with high exposures to alcohol, we were unable to describe the dose-response curve fully. It should be noted, however, that an inverse association among women has been reported previously at alcohol consumption levels comparable with those seen in our population (16). Finally, given the fact that 99 percent of the participants in our study were White, the current results may have limited generalizability to other racial/ethic groups.

Strengths of this study include the use of a Surveillance, Epidemiology, and End Results tumor registry for ascertainment of cases, a randomly selected control population representative of the population at large, and high participation rates among both cases and controls. An additional strength over previous investigations was our ability to adjust adequately for a wide variety of potential confounding factors.

In this population-based case-control investigation, we report further evidence that alcohol consumption decreases the risk of RCC among women but not among men. Our ability to show that the association remains after multivariate adjustment for several new confounding factors (i.e., diet, physical activity, and family history) strengthens support for a true association.

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